Sub F'1 26. (New) The process of claim 25, wherein the composition is a pharmaceutical composition containing GMP as an antithrombotic agents

REMARKS

The courtesies extended by Examiner David Lukton to Applicants' representative, Rodney Fuller, during the interview on November 4, 2002 are noted and appreciated. The comments and amendments presented herein are substantially the same as those that were presented and discussed at the interview.

Claims 1, 4, 6, 12 and 19 are amended, new claims 24-26 are added, and claims 5 and 20 are cancelled herein. Claims 1-4, 6-19, 21-26 appear in this application for the Examiner's review and consideration. The amendments to the claims and the addition of new claims 24-26 are fully supported by the specification and original claims. No new matter has been added.

Specifically, claims 1, 6, 12, and 19, have been amended as suggest by the Examiner during the interview of November 4, 2002 to more clearly recite the Applicants' invention and are supported by the specification at page 7, lines 7-22 and by the Examples. The amended claims are directed to a process for obtaining a fraction of lactic raw material enriched in GMP. These amendments were made to clarify that the GMP obtained from the lactic raw material does not have to be 100% GMP and may contain other components of the lactic raw material. It is preferred, however, that the GMP enriched fraction obtained from the lactic raw material contain less than 1% by weight of fat, less than 0.2% by weight of lactose, and less than 3% by weight of true whey products.

New claim 24 is based on now cancelled claim 5 written in independent form as suggested by the Examiner on page 4 of the Office Action. The step of treating the resin with an alkaline material is used to prepare the resin for absorption of GMP from the deionized lactic raw material. There is nothing contradictive about this step, as the alkaline material is not added to the lactic raw material and therefore would not affect the pH of the lactic raw material as erroneously suggested by the Examiner in the Office Action.

New claims 25 and 26 are added as suggested by the Examiner on page 4 of the Office Action. New claims 25 and 26 are directed to a process for preparing a composition that contains GMP and a pharmaceutically acceptable carrier. They are supported by the specification and original claims as filed, for example at page 7, lines 23-30, and by claims 19 and 20.

Claims 1, 12, and 20 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification as set forth on pages 2-3 of the Office Action.

Claim 20 has been cancelled.

Claims 1 and 12 have been amended. Newly amended claims 1 and 12 are directed to a process for obtaining a fraction of a lactic raw material enriched in GMP. To obtain the fraction of the lactic raw material enriched in GMP, the lactic raw material is first deionized to create a substantially deionized lactic raw material. The substantially deionized lactic raw material is than contacted with an anionic resin having a hydrophobic matrix. The anionic resin absorbs the GMP from the lactic raw material, leaving a treated liquid material (the fraction from which the GMP has been removed). The resin having absorbed GMP is then separated from the treated liquid material and the resin is separated from the GMP enriched fraction. Once separated from the resin, the GMP enriched fraction can be used, for example, in a food composition or it can be further processed, for example, by freeze-drying, etc, before use. The presently claimed invention is described in the specification in such a way that not only would one skilled the art reasonably believe that the Applicants were in possession of the claimed invention at the time of filing, but they would also be enabled to obtain a fraction of a lactic raw material enriched in GMP.

Therefore, Applicants respectfully request the Examiner withdraw the rejection under 35 U.S.C. §112, first paragraph.

Claims 1-13 and 20 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite, for the reasons set forth on pages 3-4, of the Office Action.

As stated above, Applicants herein have amended 1, 6, and 12, which are now directed to a process for obtaining a fraction of a lactic raw material enriched in GMP. The newly amended claims are definite and properly set forth the steps necessary to successfully obtain a fraction of a lactic raw material enriched in GMP.

Claim 4 has been amended in an effort to expedite the allowance of the claims to delete reference to adding calcium ions to the lactic raw material. The step is not essential in the presently claimed invention and is more closely directed to preparation of specific lactic raw materials for use in the inventive process.

Claim 5 has been cancelled and rewritten in independent form as suggested by the examiner and appears herein as new claim 24.

Claim 20 has been cancelled.

Finally, Applicants respectfully disagree with that the phrase "about 10-23%" renders claim 3 indefinite. The term "about" is fully supported by the specification, for example, at page 3, line 5, and is a commonly used term in many issued patents. The term "about" as used in claim 3, does not render the claim indefinite to one skilled in the art, but simply signifies to one skilled in the art that an exact amount is not critical to the successful use of the inventive process, but that an approximate amount may be successfully used.

In view of the amendments and remarks above, Applicants, respectfully request that the Examiner withdraw the rejection of Claims 1-13 and 20 under 35 U.S.C. §112, second paragraph.

Claims 1-3 and 5-13 are rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 5,434,250 to Shimatani for the reasons set forth on pages 5-7 of the action. Applicants traverse.

Applicants invention is directed to a process for obtaining a fraction of lactic raw material enriched in GMP. The claimed process involves the steps of:

deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature **to remove GMP** from the substantially deionized lactic raw material and to obtain a treated liquid material;

separating the resin from the treated liquid material; and

separating the GMP enriched fraction from the resin.

In contrast, Shimatani discloses and claims a process for obtaining sialic acids. The process taught by Shimatani produces a sialic acid in a mixture composed of sialic acid-bound oligosaccharides, sialic acid-bound peptides and sialic acid bound lipids (Claim 1 and column 4, lines 8-11). The dissimilar purposes of Shimatani's process and Applicants' process are evidenced in the divergent steps required by each process and the different end products produced by each.

Shimatani's sialic acid removal process comprises the steps of (1) acidifying whey to a pH of 2-5; (2) contacting the acidified whey with a cation exchanger to produce exchanger-passed solution ("EPS"); and (3) concentrating and/or desalting the EPS, wherein GMP is still part of the EPS.

Shimatani fails to teach or suggest Applicants' process, in particular, the step of **removal of GMP from the deionized lactic raw material by contacting the material with an anionic resin having a hydrophobic matrix.** Evidence of this fact can be found for example at column 2, lines 25-30, wherein the exchanger-passed solution can be adjusted to a pH below 4 and ultrafiltrated to **remove lactose, ash, and GMP** to obtain sialic acid. Because Shimatani fails to teach or suggest the step of removing GMP from deionized lactic raw material by contacting it with an anionic resin, the steps of Applicants' process that follow are also not taught, for example, the step of separating the anionic resin having absorbed GMP from the treated liquid material, followed by separating the GMP fraction from the resin.

Applicants' respectfully request that the obviousness rejection be withdrawn in view of the fact that Shimatani fails to teach or suggest all the steps of Applicants' process of obtaining a fraction of lactic raw material enriched in GMP.

The Examiner further rejects, Claims 1-3 and 5-13 under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 5,434,250 to Shimatani in view of Marshall (Ref. AL), for the reasons set forth on pages 7-8. Applicants traverse this rejection.

As discussed above, Shimatani fails to teach or suggest the steps of Applicants' process. Marshall fails to remedy the deficiencies of Shimatani. Marshall does teach the fact that GMP is a useful peptide, but fails to teach or suggest a method of obtaining GMP. Due to the fact that neither Shimatani nor Marshall suggest alone or in combination the steps of Applications' process, the rejection of Claims 1-3 and 5-13 under 35 U.S.C. §103(a) should be withdrawn.

The Examiner further rejects, Claims 1-3 and 5-13 under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 5,278,288 to Kawasaki, for the reasons set forth on page 8. Applicants' traverse.

Kawasaki is directed to a process of producing κ-casein glycomacropeptides. The process of Kawasaki involves the steps of contacting milk raw materials containing the 1/2 casein glycomacropeptide with a cation exchanger to absorb a fraction of said raw milk material on said ion exchanger; and concentrating and desalting the collected fraction which **has not been absorbed** on the cation exchanger to obtain the κ-casein glycomacropeptides. The process of Kawasaki specifically teaches and requires that the fraction **not absorbed** on the ion exchanger (the filtrate) should be collected as it contains the κ-casein glycomacropeptides.

In contrast, Applicants' process, as explained in more detail above, requires the substantially deionized lactic raw material to be contacted with **an anionic resin having a hydrophobic matrix to remove GMP from the lactic raw material.** In Applicants' process the GMP enriched fraction **is absorbed** on the anionic resin. Once the GMP is absorbed on the anionic resin, the filtrate and the resin (GMP bound) is separated, followed by the separation of the GMP enriched fraction from the resin. In Applicants' presently claimed process, the anionic resin acts to remove GMP from the lactic raw material. This step of Applicants' process and the steps that follow, are not taught or suggested by Kawasaki.

Therefore, the obviousness rejection based on Kawasaki should be withdrawn.

The Examiner further rejects, claim 20 is rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 5,434,250 to Shimatani in view of U.S. Patent No. 5,063,203 to Drouet or in the alternative over U.S. Patent No. 5,278,288 to Kawasaki in view of U.S. Patent No. 5,063,203 to Drouet for the reasons set forth on pages 8-9.

Claim 20, has been cancelled and rewritten as new claims 25 and 26 as suggested by the Examiner. As explained above in detail, neither Kawasaki nor Shimatani teach or suggest Applicants' presently claimed process. The references fail to teach the steps of Applicants' presently claimed process, in particular the step of contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix **to remove GMP** from the lactic raw material.

Drouet does nothing to remedy the deficiencies of Kawasaki and Shimatani. Drouet simply discloses that GMP inhibits thrombosis, but does not disclose any process of obtaining GMP.

Therefore, the 35 U.S.C. §103(a) is inappropriate and should be withdrawn.

In view the foregoing remarks and amendments it is believed that the entire application is now in condition for allowance. Should any issues remain please call Allan Fanucci at (212) 294-3311 or Rodney Fuller at (202) 371-5838 in order to expedite the allowance of all the claims in this application.

Should any additional fees be due, please charge them to Winston & Strawn Deposit Account No. 501-814.

Respectfully submitted,

Date: 11/12/02

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APPENDIX A - PRESENTLY PENDING CLAIMS

1. (Three Times Amended) A process for obtaining a fraction of a lactic raw material enriched in glycomacropeptide or caseinoglycomacropeptide ("GMP") comprising the steps of:

deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material;

separating the resin from the treated liquid material; and

separating the GMP enriched fraction from the resin.

2. The process according to claim 1 wherein the lactic raw material is one of sweet whey obtained after separation of casein coagulated with rennet, a concentrate of sweet whey, a sweet whey or such a whey demineralized to by electrodialysis, ion exchange, reverse osmosis, electrodeionization or a combination of these procedures, a concentrate of sweet whey demineralized by electrodialysis, ion exchange, reverse osmosis, electrodeionization or a combination of these procedures, a concentrate of proteins of substantially lactose-free sweet whey obtained by ultrafiltration, followed by diafiltration (ultrafiltration with washing), mother liquors of the crystallization of lactose from sweet whey, a permeate of ultrafiltration of a sweet whey, the product of hydrolysis, by a protease, of a native casein obtained by acid precipitation of skimmed milk with an inorganic acid or by biological acidification, where appropriate with addition of calcium ions or alternatively of a micellar casein, obtained by microfiltration of a skimmed milk, the product of hydrolysis of a caseinate by a protease.

3. The process according to claim 1 wherein the lactic raw material is sweet whey having a solids content of about 10 to 23 percent by weight.

4. (Twice Amended) The process according to claim 1 wherein the lactic raw material is a liquid or a dispersion of solids in a liquid.

5. (Cancelled)

6. (Three Times Amended) A process for obtaining a fraction of lactic raw material enriched in glycomacropeptide or caseinoglycomacropeptide ("GMP") comprising the steps of:

deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material, wherein the substantially deionized lactic raw material contacts the resin in a gently stirred reactor at a temperature of less than 50°C for one to ten hours to adsorb the GMP onto the resin;

separating the resin from the treated liquid material; and

separating the GMP enriched fraction from the resin.

7. The process according to claim 6 wherein the reactor is at a temperature between 0°C and 15°C and the resin is basic and in macroporous or macrocross-linked gel form.

8. The process according to claim 1 wherein the substantially deionized lactic raw material contacts the resin until the treated liquid material attains a constant pH of between about 4.5 to 5.5.

9. A process for the extraction and removal of glycomacropeptide or caseinoglycomacropeptide ("GMP") from a lactic raw material comprising the steps of:

deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to

remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material;

separating the resin from the treated liquid material;

concentrating the treated liquid material by evaporation and drying; and

recovering GMP by separating it from the resin.

10. The process according to claim 9 wherein the step of separating the resin from the treated liquid material is accomplished by filtration or centrifugation and the treated liquid material is dried by spray drying.

11. The process according to claim 1 wherein the anionic resin and the deionized lactic raw material are present in a ratio by volume of between 1:1 and 1:30.

12. (Twice Amended) The process according to claim 1, wherein the step of separating the GMP enriched fraction from the resin is accomplished by washing the resin with demineralized water;

desorbing the GMP from the resin by washing the resin with an acidic, basic or saline aqueous solution rinse;

washing the resin with demineralized water;

combining the eluate and the washings;

demineralizing the combined eluate and washings by ultrafiltration or nanofiltration on a membrane with a mean cut-off region of about 3000 daltons to obtain a retentate and filtrate; and

recovering the GMP enriched fraction as the retentate; and

optionally freeze-drying the recovered retentate.

13. The process according to claim 12 wherein the basic aqueous solution comprises NaOH, KOH or $Ca(OH)_2$, in a concentration of less than 8%.

14. The process of claim 1 wherein the treated liquid material has an amino acid profile that is reduced in threonine and enriched in aromatic amino acids and tryptophan relative to the lactic raw material.

15. The process of claim 14 wherein, relative to the lactic raw material, the threonine content is reduced by about 15 to 40%, and the aromatic amino acids and tryptophan are increased by about 20 to 60%.

16. The process of claim 14, wherein the treated liquid material is included in an infant or dietetic product as protein raw material.

17. The process of claim 9 wherein the treated liquid material is included in an infant or dietetic product as protein raw material.

18. The process of claim 10 wherein the dried treated liquid material is included in an infant or dietetic product as protein raw material.

19. (Twice Amended) The process of claim 1 wherein the GMP enriched fraction obtained therefrom includes less than 1% by weight of fat, less than 0.2% by weight of lactose, and less than 3% by weight of true whey products and is included with a carrier in a composition.

20. (Cancelled)

21. The process of claim 19 wherein the composition is a food composition containing the GMP as an emulsifying, gelling or foaming agent.

22. The process of claim 19 wherein the composition is a dental composition containing the GMP as an agent against plaque and caries.

23. The process according to claim 12, further comprising the step of freeze-drying the retentate.

24. (New) A process for obtaining a fraction of a lactic raw material enriched in glycomacropeptide or caseinoglycomacropeptide ("GMP") comprising the steps of:

deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

treating the resin with an alkaline material;

contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material;

separating the resin from the treated liquid material; and

separating the GMP enriched fraction from the resin.

25. (New) A process for preparing a composition that contains glycomacropeptide or caseinoglycomacropeptide ("GMP") in combination with a pharmaceutically acceptable carrier, said process comprising the steps of:

(a) deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

(b) contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material;

(c) separating the resin from the treated liquid material;

(d) separating the GMP enriched fraction from the resin; and

(e) combining the GMP of step (d) with a pharmaceutically acceptable carrier.

26. (New) The process of claim 25, wherein the composition is a pharmaceutical composition containing GMP as an antithrombotic agents.

APPENDIX B - MARKED COPY OF CLAIMS

1. (Three Times Amended) A process for obtaining a fraction of a lactic raw material enriched in [the extraction of] glycomacropeptide or caseinoglycomacropeptide ("GMP") [from a lactic raw material] comprising the steps of:

deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material;

separating the resin from the treated liquid material; and

separating [recovering] the GMP enriched fraction [by separating it] from the resin.

4. (Twice Amended) The process according to claim 1 wherein the lactic raw material is a liquid or a dispersion of solids in a liquid [and which further comprises adding calcium ions to the lactic raw material after the deionizing step].

6. (Three Times Amended) A process for obtaining a fraction of lactic raw material enriched in [the extraction of] glycomacropeptide or caseinoglycomacropeptide ("GMP") [from a lactic raw material] comprising the steps of:

deionizing a lactic raw material for a time sufficient to obtain a substantially deionized lactic raw material having a pH of about 1 to 4.5 with the pH being adjusted, if necessary, to the recited range;

contacting the substantially deionized lactic raw material with an anionic resin having a hydrophobic matrix for a sufficient amount of time and at a sufficient temperature to remove GMP from the substantially deionized lactic raw material and to obtain a treated liquid material, wherein the substantially deionized lactic raw material contacts the resin in a gently stirred reactor at a temperature of less than 50°C for one to ten hours to adsorb the GMP onto the resin;

separating the resin from the treated liquid material; and

separating [recovering] the GMP enriched fraction [by removing it] from the resin.

12. (Twice Amended) The process according to claim 1, wherein the step of separating [removing] the GMP enriched fraction from the resin is accomplished by washing the resin with demineralized water;

desorbing the GMP from the resin by washing the resin with an acidic, basic or saline aqueous solution rinse;

washing the resin with demineralized water;

combining the eluate and the washings;

demineralizing the combined eluate and washings by ultrafiltration or nanofiltration on a membrane with a mean cut-off region of about 3000 daltons to obtain a retentate and filtrate; and

recovering the GMP enriched fraction as the retentate; and

optionally freeze-drying the recovered retentate.

19. (Twice Amended) The process of claim 1 wherein the GMP enriched fraction obtained therefrom includes less than 1% by weight of fat, less than 0.2% by weight of lactose, and less than 3% by weight of true whey products and is included with a carrier in a composition.